Title: Determinants of prescribing potentially inappropriate medications in a nationwide cohort of community dwellers with dementia receiving a comprehensive geriatric assessment

Running title: Inappropriate prescribing in dementia utilizing the interRAI dataset

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Abstract:

Objective: To identify the prevalence and predictors of prescribing potentially inappropriate medications (PIMs) in a nationwide cohort of community dwellers with dementia requiring complex care needs.

Methods: A cross-matched data of the International Resident Assessment Instrument-Home Care (9.1) (interRAI-HC) and~~with~~ prescribing data obtained from the Pharmaceutical Claims Data Mart (Pharms) extract files for older adults (≥65 years) requiring complex care needs was utilized for this study. The 2015 Beers criteria were applied to identify the prevalence of PIMs in older adults with dementia. Sociodemographic and clinical predictors of PIMs were analysed using a logistic regression model.

Results: The study population consisted of 16,568 individuals who had their first interRAI assessment from 1st January 2015 to 31st December 2015. The estimated prevalence of dementia was 13.2% (2,190/16,568). 66.9% (1,465/2,190) of the older adults diagnosed with dementia were prescribed PIMs, of which anticholinergic medications constituted 59.6% (873/1,465). Males and individuals who were prescribed a greater number of medications were more likely to be prescribed PIMs. Individuals over 85 years of age, Māori ethnic group of individuals, older adults who were being supervised with respect to their activities of daily living, and individuals who reported good or excellent self reported health, had a lesser likelihood of being prescribed PIMs.

Conclusion: We found that PIMs are prescribed frequently in older adults with dementia. Comprehensive geriatric assessments can serve as a potential tool to decrease the occurrence of PIMs in vulnerable groups with poor functional and cognitive status.

Key words: Dementia, potentially inappropriate medications, interRAI, prescribing in older adults

Key Points:

The 2015 Beers criteria and interRAI assessments were used to determine the prevalence and predictors of prescribing potentially inappropriate medications (PIMs) in older adults diagnosed with dementia, and having complex care needs.

There was a high prevalence of PIMs in older adults with dementia. ~~–~~Anticholinergic medications comprised the most commonly prescribed PIMs. Sociodemographic factors including younger age, male gender, and New Zealand European ethnicity; and clinical factors like the increased number of medications prescribed, functional status, and self-reported health influenced the prescription of PIMs in this vulnerable population.

A due consideration of these attributes while prescribing may aid in reducing the prescribing of PIMs in individuals with dementia.

Introduction:

Dementia is one of the principal syndromes linked with disability and dependence among older adults and is a major challenge to individuals, communities, and societies globally.[1] The global incidence of dementia is expected to rise to 81 million by 2040, primarily due to the progressive nature of the disorder, which involves worsening of neurocognitive impairment and loss of basic functions in daily life.[2-4] In 2016, the estimated prevalence of dementia in New Zealand (NZ) was more than 62,000, which is predicted to increase to 170,000 in 2050.[5] One in every four 'international Resident Assessment Instrument- Home Care' (interRAI-HC) evaluated individuals in 2016-17 in NZ were diagnosed with dementia, of which 35% needed extensive assistance or were completely dependent, and 30% ~~had~~ showed daily episodes of disturbing behaviours, like wandering or being abusive.[6] The interRAI was developed by an international collaboration of experts and shows good inter-rater reliability. The interRAI assessors who conduct the assessments are trained in a quality assurance programme conducted by the Ministry of Health, NZ. A national competency framework supports and promotes the quality assurance programs for the interRAI assessments.[8] The interRAI-HC tool gathers information on physical, mental, social, and cognitive domains of the health of residents/clients living in home care settings.[8]

Beers et al have defined potentially inappropriate medications (PIMs) as the prescription of medications, where the risks outweigh clinical benefits, particularly when there is safer or more effective alternative therapy for the same condition.[9] A study conducted in rural community-dwelling older adults in the United States of America (USA), utilizing the Beers criteria ~~has~~

found that half of the population of older adults utilized over-the-counter and prescribed inappropriate medications.[10] Prescribing medications for older adults with dementia is challenging because of the risks associated with cognitive decline, behavioural and psychological disturbances, prescription of multiple medications, and their associated costs.[12,13] Older adults with dementia also experience a greater sensitivity to the adverse effects of medications acting on the central nervous system.[14,15] Long-term utilization of medications in older individuals with impaired physical and cognitive function has been associated with increased risks of hospitalization and mortality.[16]

The 2015 Beers Criteria is often used as a tool for assessing the appropriateness of prescribing medications in the geriatric population.[17] A systematic review among older adults with cognitive impairment and dementia reported a varied prevalence of prescription of PIMs of 10.2%–56.4% across Europe, Australia, and the United States; and the Beers criteria were applied for assessing PIMs in ~~the~~ majority of the studies.[18] Another recent literature review reported that among the five studies conducted in ambulatory home-dwelling patients diagnosed with dementia that used the Beers criteria, the prevalence of PIMs use ranged from 16.2% to 33%, and PIMs were found to be associated with the gender, ethnicity, number of medications prescribed, and varied medical conditions.[19] An understanding about the prevalence and determinants of PIMs can help prevent adverse effects, and improve the quality of prescribing in this vulnerable age-group. To our knowledge, this is the first study conducted to evaluate the predictors of prescribing PIMs in older adults with dementia receiving comprehensive geriatric risk assessments. These assessments capture a suite of sociodemographic and clinical variables that have not been previously investigated. The study aims to identify the prevalence and associations of prescribing PIMs in a nationwide cohort of community dwellers with dementia. The overarching objective of the study is to identify the factors associated with inappropriate prescribing in older adults diagnosed with dementia, identified by the 2015 version of Beers criteria, by multinomial regression, utilizing the 2015 interRAI dataset.

Materials and Methods:

The Human Ethics Committee, University of Otago, NZ has approved the proceedings of the study (ethical approval number 15/CEN/45/AM02).

Data source: The international Resident Assessment Instrument-Home Care (9.1) (interRAI-HC) dataset is a comprehensive geriatric risk assessment for community-dwelling older adults with complex care needs needing publicly funded long-term community services or aged residential care in NZ.[20] In NZ, a standardized interRAI-HC has been implemented for conducting all community care assessments in older adults requiring publically funded long-term community services or aged residential care.[21] Assessors in District Health Boards throughout NZ utilize this standardised interRAI-HC assessment to assist in defining the level of support required for the geriatric population.[20] Older adults are referred by a health practitioner to have their health requirements assessed by the trained interRAI-HC assessors. Assessors visit the individuals at their residence to develop individualized treatment plans according to a standardized protocol.[22] Once the participating individuals consent to the de-identified interRAI-HC data being used for planning and research purposes, the information is then collated into the electronic interRAI-HC database, maintained by New Zealand's Technical Advisory Services (TAS) to provide facts and figures at the provider, regional and national level.[22] The interRAI-HC assessments provide information on 20 domains, including social demographics, medical ailments, frailty, cognitive and physical function.[21] The interRAI database is linked to various NZ Ministry of Health nationwide collections, including prescription use (the Pharms database), hospital discharges (National Minimum Dataset), laboratory collections and mortality data, among others.[21] The information on all the prescription claims funded by PHARMAC (Pharmaceutical management agency) was sourced from the Pharmaceutical Claims Data Mart (Pharms) extract files 2015, prepared by community pharmacists, and includes the sociodemographics and medication details of the individuals.[24] The cross-matched 2015 interRAI-Pharms dataset was utilized for the present study.

Study population: The eligible study population comprised community dwellers (≥65 years of age) in NZ who have undergone the first interRAI comprehensive geriatric risk assessment in 2015. The present study had a retrospective design, tracking the prevalence of PIMs and dementia, and delineating the factors associated with prescription of PIMs in dementia in older individuals. The personal information of the individuals is de-identified in the dataset.

PIMs exposure: PIMs were defined according to the list of medications to be avoided in individuals diagnosed with dementia as per the 2015 Beers criteria[25] developed by the American Geriatrics Society; which comprised the prescription of psychotropics, including

antipsychotics, medications with anticholinergic properties, benzodiazepines, nonbenzodiazepines, benzodiazepine receptor agonist hypnotics, and H_2 receptor antagonists **(Table 1)**. We have excluded medications listed under the 2015 Beers criteria which were not available or not subsidized in NZ (**Appendix 1)**.

Diagnosis of dementia: Dementia was diagnosed by the Minimum Data Set (MDS) Cognitive Performance Scale (CPS).[26] The CPS is a valid and reliable seven-point hierarchical scale derived from the MDS that rates impairment from intact memory to very severe memory loss.[27] The CPS collates data on comatose status, short-term memory, cognitive skills for daily decision-making, being understood by others, and self-performance in eating;, with scores ranging from 0 (intact memory) to 6 (very severe memory impairment). The CPS has been shown to be highly correlated with the Mini-Mental State Examination in a number of validation studies.

Covariates: The individuals were grouped according to age: 65-74 years, 75-84 years, 85-94 years, and 95 years and above. Based on the literature review of known predictors of inappropriate prescribing in older adults with and without dementia, explanatory variables that were tested for their influence on prescribing patterns were:

1. **Sociodemographics:** Age [30], gender [30] ethnicities [31], marital status [30], living arrangements [32,33], alcohol intake [34], and smoking history [35].
2. **Clinical:** Activities of daily living [30,36], self-reported health [30], hospitalization [32,36], and number of medications.[37,38]

Statistical analysis: The potential impact of different explanatory variables on the outcome variable (PIMs) was analysed using logistic regression models.

Individuals with a diagnosis of dementia were flagged as a binary variable; those with the diseased condition were coded as 1, the coding for no dementia was 0. Descriptive analysis was conducted utilizing the IBM SPSS version 24. Logistic regression analysis was performed using StataCorp® Release 14.2. We utilized the 'STrengthing the Reporting of Observational studies in Epidemiology' (STROBE) guidelines (www.strobe-statement.org) as the research reporting guiding principle[39] **(Appendix 2)**

Results:

The current analysis is based on data collected from 16,568 Home-Care assessments from 1st January 2015 to 31st December 2015, who have received at least one prescription medication funded by PHARMAC. Our observations suggest that the female population comprised 60.1% (9,964). The mean (SD) age of the population was 82.35 (7.6) years. Individuals of all ethnicities were included in the study. NZ Europeans and Māori were studied particularly, as they represent the largest ethnicities in NZ.[31] 13.2% (2,190) of the study population was diagnosed with dementia. Dementia was marginally more prevalent in males (14.6%) compared to females (p=0.001), and among the Māori ethnicity (16.6%). The sociodemographic characteristics of the study population are depicted in **Table 2**, which also displays the associations of PIMs with the corresponding 95% confidence interval (CI) ($p<0.05$), after adjustment for confounders, in individuals diagnosed with dementia. Overall, we observed that 66.9% (1,465/2,190) of the older adults diagnosed with dementia were prescribed PIMs, of which 59.6% (873/1,465) constituted anticholinergic inappropriate medications. Overall, 39.9% (873/2,190) of the individuals diagnosed with dementia were prescribed anticholinergic PIMs **(Figure 1)**.

Sociodemographic predictors: Individuals over 85 years of age were less likely to be prescribed PIMs, compared to individuals aged 65-74 years (aOR=0.64, CI=0.53, 0.77 for individuals aged 85-94 years, aOR=0.53, CI=0.38, 0.73 for individuals over 95 years). Males were more likely to be prescribed PIMs (aOR=1.24, CI=1.09, 1.41) compared to females. The Māori ethnic group (aOR=0.59, CI=0.47, 0.76) and the other ethnicity groups (aOR=0.68, CI=0.54, 0.87) were less likely to be prescribed PIMs, compared to the NZ Europeans.

Clinical factors associated with PIMs

Older adults who were prescribed a greater number of medications were more likely to be prescribed PIMs (aOR=1.15, CI=1.14, 1.16), compared to those prescribed a single medication. With respect to the activities of daily living, the older adults who were being supervised (aOR=0.83, CI=0.69, 0.99) were less likely to be prescribed PIMs, compared to individuals who were independent in their self-performance and capacity. Older adults who reported excellent (aOR=0.62, CI=0.43, 0.89) and good self-health (aOR=0.65, CI=0.49, 0.85) had a lesser likelihood to be prescribed PIMs, compared to those who reported poor self-health.

Discussion:

We reported the prevalence of prescription of PIMS and identified the sociodemographic and clinical variables associated with the prescription of PIMs among community-dwelling older adults with dementia.

Several studies investigating PIMs in older individuals have been carried out in NZ that made use of the Beers criteria, and have focused on community-dwelling or hospitalized older adults.[31,35,40] This study appears to be the first to apply the 2015 Beers criteria to examine the associations of inappropriate prescribing exclusively in community-dwelling older individuals with dementia in NZ, who have received a comprehensive geriatric risk assessment.

The NZ interRAI annual report 2016-17[6] noted a 1.2 times higher prevalence of dementia in males, compared to females, findings consistent with those in our study. Likewise, in the present study, male individuals diagnosed with dementia were more prone to be prescribed PIMs, compared to females, similar to the findings of a recent study in Finland[41] which reported the male gender as a risk factor for initiation of PIMs in community-dwelling older adults with Alzheimer's disease; and the research conducted in Korea which analysed the trends in prescribing of atypical antipsychotics in geriatric patients with dementia.[42] Numerous studies have reported a higher rate of inappropriate medication use in older women than in men of the same age-group [43-45], although the clinical relevance of this association remains uncertain.[46]

Our study observed a high prevalence of dementia in the Māori group, comparable to that observed in a study conducted in NZ to assess an indigenous approach for the diagnosis and management of dementia[47], and to the findings of the NZ interRAI annual report 2016-17.[6] It has been observed that the Māori population over the age of 50 have worse health outcomes and a greater burden of chronic ailments than non-Māori of the same age-group.[48] The prevalence of PIMs (68.4%) in NZ Europeans with dementia exceeded the occurrence in all other ethnic groups of individuals, identical to other PIMs prevalence studies in the geriatric age group conducted in NZ.[31,40] This could be attributed to NZ Europeans being the predominant ethnic group in New Zealand, comprising 71.2% of the country's inhabitants.[49]

A higher proportion (72.3%) of relatively younger group (65-75 years) of individuals with dementia were prescribed PIMs, which reflects the findings of the study performed by Hyttinen et al to evaluate PIMs prevalence in community-dwelling older adults with and without

Alzheimer's Disease[41]. These findings could potentially be attributed to prescriber awareness concerning the prescription of PIMs in individuals of the older age group.[50]

There was a high prevalence of PIMs (66.9%) in older adults diagnosed with dementia in our study, comparable to the prevalence (62%) in a study conducted in community-dwelling older adults in the USA.[51] This is a significant finding of our study. Similarly, researchers in Australia[52] reported a prescription of at least one PIM as 56.4% among individuals with dementia living in residential aged care facilities. A study of six residential care homes in England[46] observed the prevalence of at least 1 PIM prescribed in 46.2% and 40.9% of the older individuals with dementia, utilizing the STOPP criteria, reviewed at two time-points, 16 weeks apart. A direct international comparison of the prevalence of PIM prescriptions with our findings is challenging because of the differences between the PIMs lists used, and the population under study. Holmes et al have developed a tool for assessment of appropriate medication prescribing in advanced dementia, in which the primary goal is palliation of symptoms.[53] There is a similar need to arrive at a global consensus through research on appropriate prescribing in older adults presenting with different stages of dementia.

One of the most significant findings of our research suggest that 59.6% of the PIMs prescribed belonged to the anticholinergic class of medications; and 39.9% of the population under study were prescribed anticholinergic medications which were termed inappropriate to prescribe in older individuals diagnosed with dementia, according to the 2015 Beers criteria.[25] Bhattacharya et al[54] reported a prevalence of 43% of anticholinergic medication prescription among elderly outpatients with dementia. A study by Somers et al[55] reported a high anticholinergic burden of PIMs in residential aged care facilities in Melbourne. A study by Cross et al[56] in Australia also reported a clinically significant anticholinergic burden in older adults attending Memory Clinics. Anticholinergic agents are specifically associated with negative outcomes in older adults diagnosed with dementia, such as risk of falls, delirium, worsening of cognitive function, and increased mortality.[54,57] The anticholinergic agents are notorious for their peripheral side effects, which include dry mouth, constipation, urinary retention, and bowel obstruction; and the central side effects such as impaired concentration, confusion, attention deficit, and impairment of memory.[54] PIMs with anticholinergic properties may also inhibit the potential benefits of cholinesterase inhibitors, which is the main pharmacological class, currently approved for the management of Alzheimer's disease.[58] Several researchers have attested that

anticholinergics may be associated with an increased risk for the development of sustained cognitive deficits, which can range from mild cognitive impairment to dementia.[59-61]

The results of the logistic regression analysis showed that the likelihood of PIMs increased with the number of medications prescribed, which is akin to the findings of the research in older people with dementia in care homes in the United Kingdom (UK),[46] the study by Wucherer et al in community-dwelling primary care patients screened positive for dementia,[62] and the research conducted in Sweden using the EU(7)-PIM list to evaluate the prevalence of PIMs in older people with cognitive impairment.[57] A study performed in UK utilizing the primary care database of anonymised electronic health records from general practice witnessed that patients over 65 years of age diagnosed with dementia, and taking multiple medications, were more likely to be prescribed antipsychotics.[63] A higher number of medications being prescribed may indicate multiple comorbidities. Drug interactions and non-adherence are other risk factors that may have adverse consequences among older adults with dementia, which are linked to a high number of prescribed medications.[57]

In our study, individuals who reported poor self-health had an increased likelihood of developing PIMs, identical to the results of a study conducted in the USA to assess potentially inappropriate anticholinergic medication use in home-dwelling older adults with dementia.[50] The Bronx Aging Study[64] revealed that patients with poor or fair ratings of self-perceived health utilized more prescription medications. Scores on self-perceived health status may be an appropriate measure of the syndrome. This is supported by the conclusion that subjects reporting fair and poor ratings on self-perceived health have increased numbers of physician visits.[64]

Contrary to the analysis of studies conducted in individuals diagnosed with dementia in Sweden[65] and in eight European countries[66], a striking result to emerge from our data is that the PIMs prevalence was higher in individuals who were functionally independent with respect to ADL.

The study found increased use of anticholinergic medicines in dementia. Several studies have shown that prescription of anticholinergic medicines can adversely impact cognition, physical function, and can also increase the risk of mortality. Future research will aim at utilizing the interRAI assessments for reducing anticholinergic medicines, and whether this leads to

improved cognitive outcomes. Further research will be undertaken to develop safer alternatives to anticholinergic medications in this vulnerable group.

Strength of the study: The strength of this study includes the use of a national comprehensive geriatric assessment, interRAI tool to record social attributes, clinical diagnosis and medication use information in a substantial number of subjects, and the inclusion of the geriatric population with dementia. Selection bias is mitigated by the wide prescription coverage in this population. Standardized interRAI HC assessments conducted by trained healthcare personnel facilitates the provision of valid clinical, social and functional data for research purposes. Various predictors incorporated in the multivariate regression model, such as living arrangements, activities of daily living, self-reported health are seldom seen in studies using administrative claims data; hence, this study provides a unique perspective to the determinants of prescription of PIMs in older adults with dementia. An additional strength is the application of the updated 2015 Beers criteria.

Limitations: The prevalence and associations of PIMs with respect to the individual psychotropic medications were not studied. It was not possible to delineate the subtypes of dementia. The retrospective analysis may not have been as competent as a prospective research in outlining the findings of the study. The geriatric risk assessments are conducted in older individuals living in the community specifically requiring complex care needs, which is different from surveyed populations of older adults living in the community. Hence, the findings of this study might not be applicable to community-dwelling older adults in various countries because of variances in the population, health systems, prescribing guidelines, and the cost of medications, as all these factors influence prescribing patterns; however, country-specific guidelines can be developed using this information. The study design is cross-sectional, hence only the associations of prescribing PIMs have been highlighted, and the causality cannot be established.

Conclusion: In the present study, we observed that the majority of the individuals diagnosed with dementia were prescribed PIMs, indicating that the quality of prescribing needs to be improved.[37] Furthermore, important sociodemographic predictors like male gender, European ethnicity, relatively younger aged individuals, and clinical predictors like the prescription of anticholinergic medications, a higher number of medications prescribed, poor self-health, and

functionally independent individuals were identified as risk factors for prescribing PIMs in older adults diagnosed with dementia. Reviewing the modifiable predictors of prescribing PIMs could significantly reduce the prevalence of inappropriate prescribing in this vulnerable population.

Statement of contributions of authors: Dr Prasad Nishtala designed the study; Dr Sharmin Bala performed the research, Dr Sharmin Bala analysed the data; Dr Prasad Nishtala and Dr Hamish Jamieson contributed new methods and models; Dr Sharmin Bala wrote the paper. All authors contributed to data interpretation, critically commented on manuscript for intellectual content, and approved the final manuscript.

Statement of human rights Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Research involving Human Participants: For this type of study formal consent is not required, since complete anonymity is maintained.

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Table 1: List of medications to be avoided in individuals diagnosed with dementia

Anticholinergics		Antipsychotics	H_2-receptor antagonists	Benzodiazapines
Chlorpheniramine	Homatropine† ~~(excludes ophthalmic)~~	Haloperidol	Cimetidine	Alprazolam
Orphenadrine	Propantheline	Trifluoperazine	Ranitidine	Lorazepam
Diphenhydramine (oral)	Chlorpromazine	Fluphenazine	Famotidine	Oxazepam
Benztropine	Clozapine	Chlorpromazine		Temazepam
Amitriptyline	Olanzapine	Thioridazine		Triazolam
Clomipramine	Thioridazine	Aripiprazole		Clonazepam
Doxepin (>6 mg)	Trifluoperazine	Quetiapine		Diazepam
Imipramine	Oxybutynin	Ziprasidone		Flurazepam
Nortriptyline	Solifenacin	Risperidone		Meprobamate
Paroxetine	Tolterodine	Clozapine		
Trimipramine	Disopyramide	Olanzapine		
Atropine† ~~(excludes ophthalmic)~~	Prochlorperazine			
Promethazine				

*†=(excludes ophthalmic)

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	Total		PIMs		
	N	(%)	aOR	95% CI	*p*-value
Age (years)					
65-74	3,048	(18.4)	1†	1	
75-84	6,776	(40.9)	0.84	(0.69, 1.01)	0.058
85-94	6,192	(37.4)	0.64	(0.53, 0.77)	0.000
95+	552	(3.3)	0.53	(0.38, 0.73)	0.000
Sex ‡					
Female	9,964	(60.1)	1†	1†	
Male	6,603	(39.9)	1.24	(1.09, 1.41)	0.001
Ethnicity					
European	14,639	(88.4)	1†	1†	
Māori	957	(5.8)	0.59	(0.47, 0.76)	0.000
Other	972	(5.9)	0.68	(0.54, 0.87)	0.002
Marital status					
Married	6,607	(39.9)	1†	1†	
Other	9,961	(60.1)	1.01	(0.80, 1.28)	0.916
Alcohol					
No	13,225	(79.8)	1†	1†	
Yes	3,343	(20.2)	1.02	(0.88, 1.19)	0.760
Smoking					
No	15,653	(94.5)	1†	1†	
Yes	915	(5.5)	0.85	(0.66, 1.09)	0.209
Living arrangements					
Alone	8,019	(48.4)	1†	1†	
Spouse only	5,447	(32.9)	1.14	(0.88, 1.50)	0.327
Other	1,292	(7.8)	0.79	(0.63, 0.99)	0.050
With child §	1,810	(10.9)	0.86	(0.71, 1.03)	0.119
Activities of daily living ¶					
Independent	9,985	(60.3)	1†	1†	
Supervision	2,143	(12.9)	0.83	(0.69, 0.99)	0.035
Limited	1,782	(10.8)	0.94	(0.76, 1.18)	0.642
Extensive	1,046	(6.3)	0.77	(0.60, 1.00)	0.053
Maximal	730	(4.4)	0.74	(0.53, 1.02)	0.066
Dependent+	880	(5.3)	0.84	(0.60, 1.16)	0.288
Self-reported health					
Poor	1925	(11.6)	1†	1†	
Excellent	522	(3.2)	0.62	(0.43, 0.89)	0.010
Good	6,806	(41.1)	0.65	(0.49, 0.85)	0.002
Fair	5,695	(34.4)	0.80	(0.60, 1.06)	0.124
Couldn't respond	1,620	(9.8)	0.82	(0.59, 1.13)	0.229
Hospitalisation					
No hospitalisation (in last 90 days)	8,602	(51.9)	1†	1†	
Other	7,966	(48.1)	1.11	(0.97, 1.27)	0.129
Dementia					

No	14,378	(86.8)	1†	1†	
Yes	2,190	(13.2)	1.17	(0.99, 1.37)	0.057
No of meds			1.15	(1.14, 1.16)	0.000

†= Reference value, ‡= 1 missing, §= not spouse / partner, ¶=2 missing.